

SUPPORT FOR THE AMENDMENTS

Claims 11-13, 27, and 33-58 were previously canceled.

Claims 3, 4, 28, and 29 are canceled herein.

Claims 1 and 15 have been amended.

The amendment to Claims 1 and 15 is supported by original Claims 1, 6, 10, and 12.

Additional support for the amendment to Claim 1 is provided by the specification as originally filed, for example, at Examples 5, 6, and 8.

No new matter has been added by the present amendments.

REMARKS

Claims 1, 2, 5-10, 14-26, and 30-32 are pending in the present application.

The objection to Claim 4 under 37 C.F.R. §1.75(c) as being an improper dependent claim is obviated by cancellation of Claim 4. Withdrawal of this ground of objection is requested.

The rejection of Claim 1-10, 14-23, and 30-32 under 35 U.S.C. §112, second paragraph, is obviated in part by amendment and respectfully traversed in part.

At the outset, Applicants note that Claims 3 and 4 have been canceled, thus obviating the criticisms related to these claims.

In the Office Action, the Examiner objects to the phrase “wherein the lysine is in a salt form salt with glutamic acid” in Claim 1. Applicants have amended this phrase to correct a typographical error by deleting the second recitation of “salt”. Thus, this phrase now recites “wherein the lysine is in a salt form with glutamic acid”. Applicants further submit that the skilled artisan would readily appreciate from the plain language of Claim 1 and the specification that this phrase relates to a salt where lysine is complexed with glutamic acid.

Accordingly, this ground of rejection should be withdrawn. Acknowledgement to this effect is requested.

The rejections of:

- (a) Claims 1-4, 6-10, 12, 14-23, and 30-32 under 35 U.S.C. §103(a) over Takagi et al,
- (b) Claims 1-4, 6-10, 12, 15-23, and 30-32 under 35 U.S.C. §103(a) over Niebes et al in view of Takagi et al,
- (c) Claims 1-10, 12, 14-23, and 30-32 under 35 U.S.C. §103(a) over Krnjevic in view of Takagi et al, and
- (d) Claims 1-10, 14-23, and 30-32 under 35 U.S.C. §103(a) over Krnjevic in view of Rath et al and Takagi et al

are respectfully traversed, but nonetheless obviated by amendment.

In the outstanding Office Action, the Examiner has maintain the rejections over: Takagi; Niebes in view of Takagi; and Krnjevic in view of Takagi and has now introduced a new rejection over Krnjevic in view of Rath and Takagi.

With respect to the rejection over Takagi, Applicants maintain that this reference fails to disclose that lysine is in salt form with glutamic acid and/or that the composition also contains arginine. Further, Takagi also fails to disclose or suggest administering a composition to a subject as defined in the presently claimed invention and the fact that something has a preventative effect has absolutely no predictive value as to its ability to treat the thing that it should to prevent.

The Examiner disagrees with the foregoing traversal alleging that Takagi disclose lysine hydrochloride (i.e., a lysine salt) and further discloses that glutamic acid may be used with lysine. Thus, the Examiner alleges that Takagi disclose a salt form of lysine and that glutamic acid is used together with the salt form of lysine. However, at no point does Takagi disclose or suggest a specific lysine/glutamic acid salt *complex* as presently claimed.

As for the failure of Takagi to disclose the subject to be treated and/or therapeutic administration. The Examiner alleges that such a method would be obvious in view of the disclosure of Takagi or at the very least it would have been within the general abilities of the artisan. In an attempt to support this allegation, the Examiner cites *KSR v. Teleflex* and makes a overly general assertion that there is a market pressure to find treatments to treat stress induced lesions.

Applicants submit that the Examiner's allegations are without merit and still fail to support a *prima facie* case of obviousness over Takagi. At best, the modifications in the cited references to arrive at the specifically claimed combination of components and treatment method amount to nothing more than an "invitation to experiment" or "obvious to try"; however, "obvious to try" has long been held *not* to constitute obviousness. *In re O'Farrell*, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

*KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, 82 USPQ2d 1385 (2007) does not eliminate the "obvious to try is not obvious" standard, as it clearly states that "obvious to try" may constitute obviousness, but only under *certain circumstances*. Specifically, *KSR* stated that the fact that a claimed combination of elements was "obvious to try" might show that such combination was obvious under 35 U.S.C. § 103, since, if there is design need or market pressure to solve problem, and there are finite number of identified, predictable solutions, person of ordinary skill in art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely product of ordinary skill and common sense, not innovation. However, the Examiner offers nothing more than

blanket assertions but fails to show how these factors apply and whether there would be such an expectation or anticipated success.

The simple fact remains that Takagi fails to disclose or suggest the administration of arginine and lysine, where lysine is in a lysine/glutamic acid salt complex, for the treatment of one or more stress-induced diseases as presently claimed. Indeed, as previously argued, the fact that something has a preventative effect has absolutely no predictive value as to its ability to treat the thing that it is supposed to prevent. For example, a bullet-proof vest may be excellent to prevent a bullet wound, but a doctor would never treat a gun-shot victim with a bullet-proof vest. The Examiner fails to show how or why the skilled artisan would believe that a preventative would also serve as a therapeutic. Thus, Applicants maintain that the present invention is not obvious in view of Takagi.

With respect to the obviousness rejections over Krnjevic in view of Takagi, with or without Rath, and the obviousness rejections over Niebes in view of Takagi, Applicants submit that these rejections are without merit. Specifically, none of Krnjevic, Niebes, or Takagi disclose or suggest the administration of arginine and lysine, where lysine is in a lysine/glutamic acid salt complex, as presently claimed.

Applicants reassert that this deficiency is fatal to the Examiner's case and further reference Example 5 (Fig. 6), Example 6 (Fig. 7), and Example 8 (Fig. 8). In the Examples lysine is in salt form with glutamic acid and the composition contains arginine. In each of these Examples, the composition of the claimed invention showed significant benefits are achieved from the present invention. In particular, note is made of the aqueous mixture of lysine glutamate salt and arginine showed significant reduction of the areas of gastric bleeding in Example 5 and significantly prolonged time duration for searching action in Example 6. Example 8 contains the following additional disclosure "additionally, it is

understood that the combined use of other specific amino acids, for example glutamic acid and arginine can further enhance the effect (of lysine)”. This effect is not found in any of Takagi et al, Niebes et al, Rath, or Krnjevic.

The Examiner disregards this showing alleging that these data fail provide any independent examples that show the results of a glutamate salt or arginine. Accordingly, the Examiner alleges that it is not possible to draw a reasonable conclusion. Further, the Examiner alleges that the results are not unexpected as it would be expected that different amino acids would have different efficacies. However, the Examiner makes no attempt to support these assertions and/or to show what result would have been expected. Certainly, even after *KSR v Teleflex*, any obviousness determination rests squarely on predictability or expectation of the result. A mere state that different amino acids would be expected to have different efficacies is not sufficient to establish that the results set forth in the present specification are “expected.”

Thus, Applicants submit that the presently claimed invention is not obvious in view of any combination of Takagi et al, Niebes et al, Rath, or Krnjevic. Nonetheless, to expedite examination of the present application, Applicants have amended Claim 1 to remove “gastric ulcers” as a class of stress-induced diseases to be treated. In the outstanding Office Action, the Examiner appears to recognize that, at best, the cited art relate to prevention or treatment of gastric lesions or gastric ulcers caused by the administration of nonsteroidal anti-inflammatory agents (alleged to be a “stressor”). Putting aside the propriety or impropriety of these allegations, Applicants submit that the cited art fail to disclose or suggest “a method of ameliorating, progress blocking, or therapeutically treating one or more stress-induced diseases comprising administering to a subject in need thereof an effective amount of a pharmaceutical composition comprising lysine and arginine, wherein said stress-induced

diseases include one or more diseases selected from the group consisting of dissociated disorders, abnormal gastric motion, and irritable bowel syndrome, wherein the lysine is in a salt form salt with glutamic acid" (Claim 1) as presently claimed. Further, Applicants submit that such a method would not be obvious.

Withdrawal of these grounds of rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, L.L.P.



Stephen G. Baxter, Ph.D.  
Registration No. 32,884

Vincent K. Shier, Ph.D.  
Registration No. 50,552

Customer Number

22850

Tel: (703) 413-3000  
Fax: (703) 413-2220  
(OSMMN 08/03)